WHAT IS CLAIMED IS:

1. A compound having the formula:

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wherein

W and X are independently selected from the group consisting of N and CH;

Y is selected from the group consisting of O, S and N(R);

wherein R is selected from the group consisting of H, CN, NO₂, (C_1 - C_{10})alkyl, (C_3 - C_{10})cycloalkyl, (C_4 - C_{10})cycloalkyl-alkyl, (C_3 -

C₁₀)alkenyl and (C₂-C₁₀)alkynyl;

Z is selected from the group consisting of H, (C_1-C_{10}) alkyl, (C_3-C_{10}) cycloalkyl, (C_4-C_{10}) cycloalkyl-alkyl, (C_2-C_{10}) alkenyl, (C_2-C_{10}) alkynyl and NR^2R^3 ;

 R^1 , R^2 and R^3 are independently selected from the group consisting of H, (C₁-C₁₀)alkyl, (C₃-C₁₀)alkenyl, (C₂-C₁₀)alkynyl, (C₁-C₁₀)heteroalkyl, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl, aryl, aryl(C₁-C₄)alkyl, aryl(C₁-C₄)heteroalkyl, heteroaryl(C₁-C₄)alkyl, heteroaryl(C₁-C₄)heteroalkyl and perfluoro(C₁-C₆)alkyl; and wherein when Z is NR^2R^3 , R^2 and R^3 can be combined to form a 5- to 7-membered heterocyclyl ring;

 R^4 is selected from the group consisting of H, (C_1-C_6) alkyl, (C_3-C_6) cycloalkyl, (C_4-C_7) cycloalkyl-alkyl, (C_2-C_6) alkenyl and (C_2-C_6) alkynyl;

A is a substituted or unsubstituted fused carbocyclic or heterocyclic ring system, said ring system being mono- or bicyclic wherein said mono- or bicyclic rings are selected from the group consisting of five- and six-membered rings that are aromatic or partially or completely saturated; and

B is a substituted or unsubstituted five- or six-membered ring which is aromatic or partially or completely saturated, containing at least one nitrogen atom, and from 0 to 3 additional heteroatoms, wherein the B ring substituents are selected from the group consisting of halogen, CF₃, CF₃O, (C₁-C₆)alkyl,

- A compound of claim 2, wherein Z is NR^2R^3 . 9.
- A compound of claim 6, wherein R⁴ is H. **10**.
- 1 11. A compound of claim 1, wherein A is selected from the group
- 2 consisting of:

- 1 **12**. A compound of claim 1, wherein A is selected from the group
- 2 consisting of:

34 wherein

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R⁵, R⁶, R⁷ and R⁸ are independently selected from the group consisting of H, halogen, CF₃, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-

halogen, CF₃, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁

C₆)heteroalkyl, (C₁-C₆)alkoxy, (C₁-C₆)thioalkoxy, amino, (C₁-

C₆)alkylamino, di(C₁-C₆)alkylamino, (C₃-C₁₀)cycloalkyl, (C₄-

C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl, (C₃-C₁₀)cycloheteroalkyl-alkyl, cyano, nitro, (C₁-C₆)acyl, (C₁-C₆)acylamino, (C₁-C₆)alkoxycarbonyl,

(C₁-C₆)alkoxycarbonyl (C₁-C₆)alkyl, CONH₂, CO-NH-(C₁-C₆)alkyl, CO-

 $N[(C_1-C_6)alkyl]_2$, SO_2NH_2 , $SO_2NH-(C_1-C_6)alkyl$, $SO_2N-[(C_1-C_6)alkyl]_2$

and (C₁-C₆)heteroalkoxy; or two adjacent R groups selected from R⁵, R⁶,

R⁷ and R⁸, can be linked together to form a new 5- or 6-membered carbocyclic or heterocyclic ring.

13. A compound of claim 12, wherein W is N; X is CH; Y is O or S; and A is selected from the group consisting of:

$$R^{6}$$
 R^{7}
 R^{8}
 R^{8}
 R^{8}
 R^{8}
 R^{8}
 R^{8}
 R^{8}

3

1

2

2

14. A compound of claim 1, wherein B contains a nitrogen atom at a position two atoms away from the atom attaching B to the remainder of the molecule.

1 15. A compound of claim 1, wherein B contains a nitrogen atom at the point of attachment of B to the remainder of the molecule.

1 16. A compound of claim 1, wherein B is selected from the group 2 consisting of 1-methylimidazol-5-yl, 1-(trifluoromethyl)imidazol-5-yl, 5-methylimidazol-

- 4 triazolyl, and 4-methyl-1,2,4-triazol-3-yl.
- A compound of claim 1, wherein B is selected from the group 1 **17**.
- consisting of substituted or unsubstituted imidazolyl, substituted or unsubstituted 2
- thiazolyl and substituted or unsubstituted triazolyl. 3
- 1 **18**. A compound of claim 13, wherein B contains a nitrogen atom at a
- 2 position two atoms away from the atom attaching B to the remainder of the molecule.
- 1 19. A compound of claim 13, wherein B contains a nitrogen atom at
- 2 the point of attachment of B to the remainder of the molecule.
- 20. A compound of claim 13, wherein B is selected from the group
 - consisting of 1-methylimidazol-5-yl, 1-(trifluoromethyl)imidazol-5-yl, 5-methylimidazol-
 - 1-vl. 5-(trifluoromethyl)imidazol-1-vl, thiazol-5-vl, imidazol-1-yl, 1-methyl-1,3,4-
 - triazolyl, and 4-methyl-1,2,4-triazol-3-yl.
 - 21. A compound of claim 13, wherein B is selected from the group
 - consisting of substituted or unsubstituted imidazolyl, substituted or unsubstituted
 - thiazolyl and substituted or unsubstituted triazolyl.
 - 22. A compound of claim 1, wherein W is N; X is CH; Y is O or S; Z
 - is H, CH₃, NH₂ or NHCH₃; R¹ is H, (C₁-C₆)alkyl, (C₁-C₁₀)heteroalkyl, (C₄-2
 - C₁₀)cycloheteroalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl, aryl(C₁-C₄)alkyl, aryl(C₁-3
 - 4 C₄)heteroalkyl, heteroaryl(C₁-C₄)alkyl, heteroaryl(C₁-C₄)heteroalkyl, or perfluoro(C₁-
 - C₆)alkyl; R⁴ is H; A represents 5

- wherein R⁶ and R⁷ are independently selected from the group consisting of 7
- H, halogen, CF_3 , CF_3O , (C_1-C_4) alkyl, (C_2-C_4) alkenyl, (C_2-C_4) alkynyl, (C_1-C_4) heteroalkyl, 8
- 9 (C₃-C₁₀)cycloheteroalkyl-alkyl and cyano; and B is a five-membered aromatic ring
- 10 system containing at least one nitrogen atom.
 - 23. A compound of claim 22, wherein Y is S.

- A compound of claim 22, wherein Z is NR^2R^3 . 1 24. A compound of claim 22, wherein Z is NH₂. 25. 1 A compound of claim 22, wherein R¹ is (C₁-C₆)alkyl, (C₁-26. 1 C_6)heteroalkyl or (C_3-C_{10}) cycloheteroalkyl-alkyl. 2 A compound of claim 22, wherein B is a five-membered aromatic 27. 1 ring system containing 1-2 nitrogen atoms and 0-1 sulfur atoms. 2 A compound of claim 27, wherein B is unsubstituted or substituted 28. 1 by (C₁-C₃)alkyl, CF₃, cyano, or halogen. 2 A compound of claim 22, wherein Z is NH₂; R⁶ is selected from the **j.** 1 **29**. Alme Sareh Marri W. Wall Book Marrie Marrie group consisting of H, halogen, CF₃, CF₃O, (C₁-C₄)alkyl, (C₂-C₄)alkenyl, (C₁-2 C₄)heteroalkyl, (C₃-C₁₀)cycloheteroalkyl-alkyl and cyano, wherein the alkyl, alkenyl and 3 heteroalkyl groups optionally bear additional substituents selected from cyano, 4 carboxamido,(C₁-C₃)alkylsulfonyl or (C₁-C₃)alkoxy; and R⁷ is selected from the group 5 6 7 1 1 2 2 consisting of H, halogen, CF₃, CF₃O, (C₁-C₄)alkyl, (C₂-C₄)alkenyl, (C₂-C₄)alkynyl, (C₁-C₄)heteroalkyl and cyano. A compound of claim 29, wherein R⁶ is selected from the group 30. consisting of CH₂(CH₂)_mCN, CH₂(CH₂)_nSO₂CH₃ and CH₂(CH₂)_nOCH₃, wherein the 3 subscript n is an integer from 0 to 2. A compound of claim 29, wherein R⁶ is 1 31. ser or ser 2
 - 1 32. A compound of claim 29, wherein R⁷ is selected from H, halogen, 2 CF₃ and (C₁-C₄)alkyl.
 - 1 33. A compound of claim 29, wherein R⁷ is methyl.
 - 1 34. A compound of claim 1, having the formula:

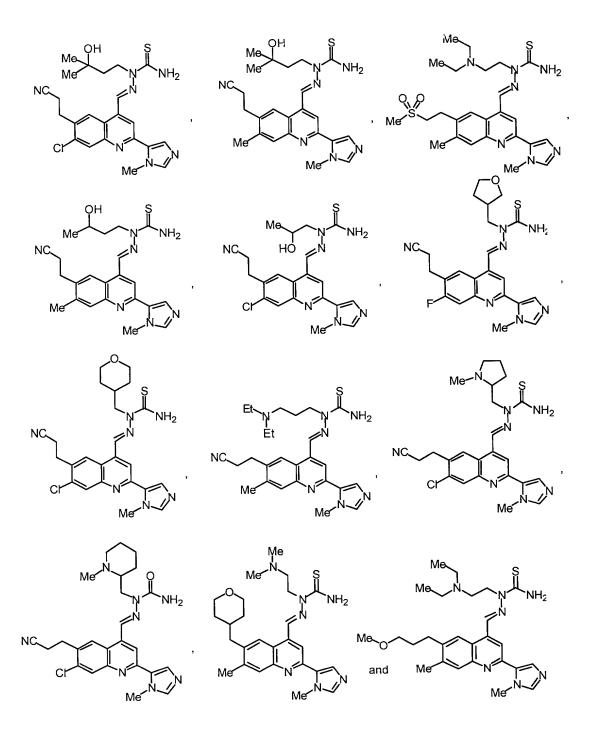
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$$R^{10} \xrightarrow{N} N \xrightarrow{N} NH_{2}$$

$$R^{9} \xrightarrow{N} R^{7} \xrightarrow{N} N \xrightarrow{N} R^{11}$$

- wherein Y is O, S or N-CN; W' is N(CH₃), N(CF₃), N(CH₂CH₃), O or S; the subscripts n 3
- and n' are independently integers from 0 to 3; R⁷is H, halogen, CF₃, CF₃O, (C₁-C₄)alkyl, 4
- (C2-C4)alkenyl, (C2-C4)alkynyl, (C1-C4)heteroalkyl or cyano; R9 is CN, CONH2, CO-NH-5
- $(C_1-C_6)alkyl, CO-N[(C_1-C_6)alkyl]_2, CO-NH-(C_1-C_6)heteroalkyl, CO-N[(C_1-C_6)alkyl)]_2$ 6
- $C_6) heteroalkyl]_2, S(O)_{n"}-(C_1-C_6) alkyl, S(O)_{n"}-(C_1-C_6) heteroalkyl, heteroaryl, (C_1-C_6) heteroalkyl)_2, S(O)_{n''}-(C_1-C_6) alkyl, S(O)_{n''}-(C_1-C_6) heteroalkyl, heteroaryl, (C_1-C_6) heteroaryl, (C_1-C_6) heteroaryl, heteroaryl, (C_1-C_6) heteroaryl, heteroaryl, (C_1-C_6) heteroaryl, het$
- C₆)alkoxy or (C₃-C₆)cycloheteroalkyl, wherein each n" is independently an integer of 0 to
- 2; R¹⁰ is NH₂, NH₋(C₁-C₆)alkyl, N[(C₁-C₆)alkyl]₂, NH₋(C₁-C₆)heteroalkyl, N[(C₁-C₆)alkyl]₂
- $C_6) heteroalkyl]_2, (C_1-C_6) heteroalkyl, \\ S(O)_{n"}-(C_1-C_6) alkyl, \\ S(O)_{n"}-(C_1-C_6) heteroalkyl, \\ aryl, \\ aryl,$
- 8 9 10 11 heteroaryl, O-(C_1 - C_6)alkyl, O-(C_1 - C_6)heteroalkyl or (C_3 - C_8)cycloheteroalkyl; and R^{11} is
 - H. CF₃, NH₂, NH- (C_1-C_6) alkyl, N[(C_1-C_6) alkyl]₂, halogen or (C_1-C_3) alkyl.
 - A compound of claim 34, wherein Y is O or S; W' is N-CH₃; n is 1 **35**.
- 2; n' is 1-3; R⁹ is cyano, CONH₂, SO₂-(C₁-C₆)alkyl, (C₁-C₆)alkoxy or (C₃-2
 - C_6)cycloheteroalkyl; R^{10} is NH- (C_1-C_6) alkyl, N[(C_1-C_6) alkyl]₂, NH- (C_1-C_6) heteroalkyl, 3
 - $N[(C_1-C_6)heteroalkyl]_2$, $O-(C_1-C_6)alkyl$, $O-(C_1-C_6)heteroalkyl$, $(C_1-C_6)alkoxy$ or $(C_3-C_6)alkyl$ 4
 - C₈)cycloheteroalkyl; and R¹¹ is H. 5
 - A compound of claim 22, wherein B contains a nitrogen atom at a **36**. 1
 - position two atoms away from the atom attaching B to the remainder of the molecule. 2
 - A compound of claim 22, wherein B contains a nitrogen atom at 1 **37**.
 - the point of attachment of B to the remainder of the molecule. 2
 - A compound of claim 22, wherein B is selected from the group 1 38.
 - consisting of substituted or unsubstituted imidazolyl, substituted or unsubstituted 2
 - 3 thiazolyl and substituted or unsubstituted triazolyl.
 - A compound of claim 22, wherein B is selected from the group 1 **39**.
 - 2 consisting of 1-methylimidazol-5-yl, 1-(trifluoromethyl)imidazol-5-yl, 5-methylimidazol-

- 3 1-yl, 5-(trifluoromethyl)imidazol-1-yl, thiazol-5-yl, imidazol-1-yl, 1-methyl-1,3,4-
- 4 triazolyl, and 4-methyl-1,2,4-triazol-3-yl.
- 1 40. A compound of claim 1, wherein Y is S; Z is NH₂ and R¹ is (C₁-
- 2 C₆)alkyl.
- 1 41. A compound of claim 40, wherein R¹ is methyl.
- 1 42. A compound of claim 1, wherein said compound is selected from the
- 2 group consisting of:



 43. A composition comprising a pharmaceutically acceptable excipient

and a compound having the formula:

wherein 4 W and X are independently selected from the group consisting of N and CH; 5 Y is selected from the group consisting of O, S and N(R); 6 wherein R is selected from the group consisting of H, CN, NO₂, (C₁-7 C₁₀)alkyl, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-8 C_{10})alkenyl and (C_2-C_{10}) alkynyl; 9 Z is selected from the group consisting of H, (C₁-C₁₀)alkyl, (C₃-C₁₀)cycloalkyl, 11 12 13 14 (C₄-C₁₀)cycloalkyl-alkyl, (C₂-C₁₀)alkenyl, (C₂-C₁₀)alkynyl and NR²R³; R¹, R² and R³ are independently selected from the group consisting of H, (C₁-C₁₀)alkyl, (C₃-C₁₀)alkenyl, (C₂-C₁₀)alkynyl, (C₂-C₁₀)heteroalkyl, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl-alkyl, 15 16 17 $(C_3\text{-}C_{10}) cycloheteroalkyl, \, aryl, \, aryl(C_1\text{-}C_4) alkyl, \, aryl(C_2\text{-}C_4) heteroalkyl, \,$ $heteroaryl(C_2\text{-}C_4) alkyl, \, heteroaryl(C_2\text{-}C_4) heteroalkyl \, \, and \, perfluoro(C_1\text{-}C_4) heteroaryl(C_2\text{-}C_4) alkyl, \, heteroaryl(C_2\text{-}C_4) heteroalkyl \, \, and \, perfluoro(C_1\text{-}C_4) heteroaryl(C_2\text{-}C_4) heteroalkyl \, \, and \, heteroalkyl \, \, an$ C₆)alkyl; and wherein when Z is NR²R³, R² and R³ can be combined to form a 5- to 7-membered ring; and wherein when Y is N(R), R and R1 are **1**8 optionally combined to form a 5- to 7-membered ring; 19 R⁴ is selected from the group consisting of H, (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, 20 (C_4-C_7) cycloalkyl-alkyl, (C_2-C_6) alkenyl and (C_2-C_6) alkynyl; 21 A is a substituted or unsubstituted fused carbocyclic or heterocyclic ring system, 22 said ring system being mono- or bicyclic wherein said mono- or bicyclic 23 rings are selected from the group consisting of five- and six-membered 24 rings that are aromatic or partially or completely saturated; and 25 B is a substituted or unsubstituted five- or six-membered ring which is aromatic or 26 partially or completely saturated, containing at least one nitrogen atom, 27 and from 0 to 3 additional heteroatoms, wherein the B ring substituents are 28 selected from the group consisting of halogen, CF₃, CF₃O, (C₁-C₆)alkyl, 29 perfluoro(C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-C₆)heteroalkyl, 30 (C1-C6)alkoxy, (C1-C6)thioalkoxy, amino, (C1-C6)alkylamino, di(C1-31

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- C₆)alkylamino, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-
- 33 C₁₀)cycloheteroalkyl, cyano, nitro, sulfonamido, (C₁-C₆)acyl, (C₁-
- 34 C₆)acylamino, (C₂-C₆)alkoxycarbonyl, (C₂-C₆)alkoxycarbonyl(C₁-
- 35 C₆)alkyl, carboxamido and (C₁-C₆)heteroalkoxy.
- 1 44. A composition in accordance with claim 43, wherein W is N and X
- 2 is CH.

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- 1 45. A composition in accordance with claim 43, wherein W is N and X
- 2 is N.
- 1 46. A composition in accordance with claim 43, wherein W is CH and
- 2 X is N.
- 1 47. A composition in accordance with claim 43, wherein W is CH and
- 2 X is CH.
- 1 48. A composition in accordance with claim 43, wherein Y is selected 2 from the group consisting of O and S.
- 1 49. A composition in accordance claim 43, wherein Y is O.
- 1 50. A composition in accordance claim 43, wherein Y is S.
- 51. A composition in accordance claim 43, wherein Z is NR²R³.
- 1 52. A composition in accordance with claim 48, wherein R⁴ is H.
- 1 53. A composition in accordance with claim 43, wherein A is selected 2 from the group consisting of:

$$R^6$$
 R^7
 R^7
 R^7

$$\mathbb{R}^7$$
 \mathbb{N}
 \mathbb{N}

2 from the group consisting of:

4 wherein

R⁵, R⁶, R⁷ and R⁸ are independently selected from the group consisting of H, halogen, CF₃, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-C₆)heteroalkyl, (C₁-C₆)alkoxy, (C₁-C₆)thioalkoxy, amino, (C₁-C₆)alkylamino, di(C₁-C₆)alkylamino, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl, (C₃-C₁₀)cycloheteroalkyl-alkyl, cyano, nitro, (C₁-C₆)acyl, (C₁-C₆)acylamino, (C₂-C₆)alkoxycarbonyl, (C₃-C₆)alkoxycarbonylalkyl, CONH₂, CO-NH-(C₁-C₆)alkyl, CO-N[(C₁-C₆)alkyl]₂, SO₂NH₂, SO₂NH-(C₁-C₆)alkyl, SO₂N-[(C₁-C₆)alkyl]₂ and (C₁-C₆)heteroalkoxy; or two adjacent R groups can be linked together to form a new 5- or 6-membered carbocyclic or heterocyclic ring.

1 55. A composition in accordance with claim 43, wherein W is N; X is 2 CH; Y is O or S; and A is selected from the group consisting of:

$$R^{6}$$
 R^{7}
 R^{8}
 R^{8}
 R^{8}
 R^{8}
 R^{8}
 R^{8}
 R^{8}

56. A composition in accordance with claim 43, wherein B contains a nitrogen atom at a position two atoms away from the atom attaching B to the remainder of the molecule.

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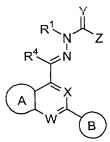
64.

an effective amount of a compound having the formula:

1	57. A composition in accordance with claim 43, wherein B contains a				
2	nitrogen atom at the point of attachment of B to the remainder of the molecule.				
1	58. A composition in accordance with claim 43, wherein B is selected				
2	from the group consisting of 1-methylimidazol-5-yl, 1-(trifluoromethyl)imidazol-5-yl, 5-				
3	methylimidazol-1-yl, 5-(trifluoromethyl)imidazol-1-yl, thiazol-5-yl, imidazol-1-yl, 1-				
4	methyl-1,3,4-triazolyl, and 4-methyl-1,2,4-triazol-3-yl.				
1	59. A composition in accordance with claim 43, wherein B is selected				
2	from the group consisting of substituted or unsubstituted imidazolyl, substituted or				
3	unsubstituted thiazolyl and substituted or unsubstituted triazolyl.				
1	60. A composition in accordance with claim 55, wherein B contains a				
2	nitrogen atom at a position two atoms away from the atom attaching B to the remainder of				
3	the molecule.				
1	61. A composition in accordance with claim 55, wherein B contains a				
2	nitrogen atom at the point of attachment of B to the remainder of the molecule.				
1	62. A composition in accordance with claim 55, wherein B is selected				
2	from the group consisting of 1-methylimidazol-5-yl, 1-(trifluoromethyl)imidazol-5-yl, 5-				
3	methylimidazol-1-yl, 5-(trifluoromethyl)imidazol-1-yl, thiazol-5-yl, imidazol-1-yl, 1-				
4	methyl-1,3,4-triazolyl, and 4-methyl-1,2,4-triazol-3-yl.				
1	63. A composition in accordance with claim 55, wherein B is selected				
2	from the group consisting of substituted or unsubstituted imidazolyl, substituted or				
3	unsubstituted thiazolyl and substituted or unsubstituted triazolyl.				

condition, said method comprising administering to a subject in need of such treatment,

A method for treating an inflammatory, metabolic or malignant



4	В		
5 wherein			
6	W and X are independently selected from the group consisting of N and CH;		
7	Y is selected from the group consisting of O, S and N(R);		
8	wherein R is selected from the group consisting of H, CN, NO ₂ , (C ₁ -		
9	C ₁₀)alkyl, (C ₃ -C ₁₀)cycloalkyl, (C ₄ -C ₁₀)cycloalkyl-alkyl, (C ₃ -		
10	C_{10}) alkenyl and (C_2 - C_{10}) alkynyl;		
<u>1</u> 11	Z is selected from the group consisting of H, (C ₁ -C ₁₀)alkyl, (C ₃ -C ₁₀)cycloalkyl,		
12	(C ₄ -C ₁₀)cycloalkyl-alkyl, (C ₂ -C ₁₀)alkenyl, (C ₂ -C ₁₀)alkynyl and NR ² R ³ ;		
= 13	R^1 , R^2 and R^3 are independently selected from the group consisting of H, (C_1 -		
11 12 13 14 15	C_{10}) alkyl, (C_3-C_{10}) alkenyl, (C_2-C_{10}) alkynyl, (C_2-C_{10}) heteroalkyl, (C_3-C_{10})		
15	C_{10})cycloalkyl, (C_4 - C_{10})cycloalkyl-alkyl, (C_3 - C_{10})cycloheteroalkyl-alkyl,		
16	(C_3-C_{10}) cycloheteroalkyl, aryl, aryl (C_1-C_4) alkyl, aryl (C_2-C_4) heteroalkyl,		
	heteroaryl(C_2 - C_4)alkyl, heteroaryl(C_2 - C_4)heteroalkyl and perfluoro(C_1 -		
17 18 19	C ₆)alkyl; and wherein when Z is NR ² R ³ , R ² and R ³ can be combined to		
19	form a 5- to 7-membered ring; and wherein when Y is N(R), R and R1 are		
20	optionally combined to form a 5- to 7-membered ring;		
21	R ⁴ is selected from the group consisting of H, (C ₁ -C ₆)alkyl, (C ₃ -C ₆)cycloalkyl,		
22	(C ₄ -C ₇)cycloalkyl-alkyl, (C ₂ -C ₆)alkenyl and (C ₂ -C ₆)alkynyl;		
23	A is a substituted or unsubstituted fused carbocyclic or heterocyclic ring system,		
24	said ring system being mono- or bicyclic wherein said mono- or bicyclic		
25	rings are selected from the group consisting of five- and six-membered		
26	rings that are aromatic or partially or completely saturated; and		
27	B is a substituted or unsubstituted five- or six-membered ring which is aromatic or		
28	partially or completely saturated, containing at least one nitrogen atom,		
29	and from 0 to 3 additional heteroatoms, wherein the B ring substituents are		
30	selected from the group consisting of halogen, CF ₃ , CF ₃ O, (C ₁ -C ₆)alkyl,		
31	$perfluoro(C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_1-C_6)heteroalkyl,\\$		
32	(C_1-C_6) alkoxy, (C_1-C_6) thioalkoxy, amino, (C_1-C_6) alkylamino, di (C_1-C_6)		

- C₆)alkylamino, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl, cyano, nitro, sulfonamido, (C₁-C₆)acyl, (C₁-C₆)acylamino, (C₂-C₆)alkoxycarbonyl, (C₂-C₆)alkoxycarbonyl(C₁-C₆)alkyl, carboxamido and (C₁-C₆)heteroalkoxy.

 A method in accordance with claim 64, wherein W is N and
- 1 65. A method in accordance with claim 64, wherein W is N and X is 2 CH.
- 1 66. A method in accordance with claim 64, wherein W is N and X is N.
- 1 67. A method in accordance with claim 64, wherein W is CH and X is 2 N.
- 1 68. A method in accordance with claim 64, wherein W is CH and X is 2 CH.
- 1 69. A method in accordance with claim 65, wherein Y is selected from 2 the group consisting of O and S.
 - 70. A method in accordance with claim 65, wherein Y is O.
- 1 71. A method in accordance with claim 65, wherein Y is S.
- 1 72. A method in accordance with claim 65, wherein Z is NR^2R^3 .
- 1 73. A method in accordance with claim 69, wherein R⁴ is H.
- 1 74. A method in accordance with claim 64, wherein A is selected from 2 the group consisting of:

$$R^{6}$$
 R^{5}
 R^{7}
 R^{7

2 the group consisting of:

4 wherein

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the their form and the same that

- R⁵, R⁶, R⁷ and R⁸ are independently selected from the group consisting of H, halogen, CF₃, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-C₆)heteroalkyl, (C₁-C₆)alkoxy, (C₁-C₆)thioalkoxy, amino, (C₁-C₆)alkylamino, di(C₁-C₆)alkylamino, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl, (C₃-C₁₀)cycloheteroalkyl-alkyl, cyano, nitro, (C₁-C₆)acyl, (C₁-C₆)acylamino, (C₂-C₆)alkoxycarbonyl, (C₃-C₆)alkoxycarbonylalkyl, CONH₂, CO-NH-(C₁-C₆)alkyl, CO-N[(C₁-C₆)alkyl]₂, SO₂NH₂, SO₂NH-(C₁-C₆)alkyl, SO₂N-[(C₁-C₆)alkyl]₂ and (C₁-C₆)heteroalkoxy; or two adjacent R groups can be linked together to form a new 5- or 6-membered carbocyclic or heterocyclic ring.
- 1 76. A method in accordance with claim 64, wherein W is N; X is CH; 2 Y is O or S; and A is selected from the group consisting of:

1 77. A method in accordance with claim 64, wherein B contains a

- nitrogen atom at a position two atoms away from the atom attaching B to the remainder of
- 3 the molecule.

1	78. A method in accordance with claim 64, wherein B contains a					
2	nitrogen atom at the point of attachment of B to the remainder of the molecule.					
1	79. A method in accordance with claim 64, wherein B is selected from					
2	the group consisting of 1-methylimidazol-5-yl, 1-(trifluoromethyl)imidazol-5-yl, 5-					
3	methylimidazol-1-yl, 5-(trifluoromethyl)imidazol-1-yl, thiazol-5-yl, imidazol-1-yl, 1-					
4	methyl-1,3,4-triazolyl, and 4-methyl-1,2,4-triazol-3-yl.					
1	80. A method in accordance with claim 64, wherein B is selected from					
2	the group consisting of substituted or unsubstituted imidazolyl, substituted or					
3	unsubstituted thiazolyl and substituted or unsubstituted triazolyl.					
1	81. A method in accordance with claim 76, wherein B contains a					
2	nitrogen atom at a position two atoms away from the atom attaching B to the remainder of					
3	the molecule.					
1	82. A method in accordance with claim 76, wherein B contains a					
2	nitrogen atom at the point of attachment of B to the remainder of the molecule.					
1	83. A method in accordance with claim 76, wherein B is selected from					
2	the group consisting of 1-methylimidazol-5-yl, 1-(trifluoromethyl)imidazol-5-yl, 5-					
3	methylimidazol-1-yl, 5-(trifluoromethyl)imidazol-1-yl, thiazol-5-yl, imidazol-1-yl, 1-					
4						
1	84. A method in accordance with claim 76, wherein B is selected from					
2	the group consisting of substituted or unsubstituted imidazolyl, substituted or					
3	unsubstituted thiazolyl and substituted or unsubstituted triazolyl.					
1	85. A method in accordance with claim 64, wherein said compound is					
2	administered orally.					
1	86. A method in accordance with claim 64, wherein said compound is					
2	administered topically.					
1	87. A method in accordance with claim 64, wherein said compound is					
2	administered intravenously or intramuscularly					

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wherein

1	88. A method in accordance with claim 64, wherein said compound is					
2	administered in combination with a second therapeutic agent, said second therapeutic					
3	agent being a member selected from the group consisting of prednisone, dexamethasone,					
4	beclomethasone, methylprednisone, betamethasone, hydrocortisone, methotrexate,					
5	cyclosporin, rapamycin, tacrolimus, antihistamine drugs, TNF antibodies, IL-1 antibodies,					
6	soluble TNF receptors, soluble IL-1 receptors, TNF or IL-1 receptor antagonists, non-					
7	steroidal antiinflammatory agents, COX-2 inhibitors, antidiabetic agents, and anticancer					
8	agents.					
1	89. A method in accordance with claim 88, wherein said administering					
2	is sequential.					

90. A method in accordance with claim 64, wherein said inflammatory, metabolic or malignant condition is selected from the group consisting of rheumatoid arthritis, inflammatory bowel disease, psoriasis, cancer, diabetes and septic shock.

91. A method for treating a condition or disorder mediated by IKK, comprising

administering to a subject in need thereof a therapeutically effective amount of a compound having the formula:

W and X are independently selected from the group consisting of N and CH;
Y is selected from the group consisting of O, S and N(R);

9 wherein R is selected from the group consisting of H, CN, NO₂, (C₁10 C₁₀)alkyl, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-

 C_{10}) alkenyl and (C_2-C_{10}) alkynyl;

Z is selected from the group consisting of H, (C₁-C₁₀)alkyl, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₂-C₁₀)alkenyl, (C₂-C₁₀)alkynyl and NR²R³;

 R^1 , R^2 and R^3 are independently selected from the group consisting of H, (C₁-C₁₀)alkyl, (C₃-C₁₀)alkenyl, (C₂-C₁₀)alkynyl, (C₁-C₁₀)heteroalkyl, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl, aryl, aryl(C₁-C₄)alkyl, aryl(C₁-C₄)heteroalkyl, heteroaryl(C₁-C₄)alkyl, heteroaryl(C₁-C₄)heteroalkyl and perfluoro(C₁-C₆)alkyl; and wherein when Z is NR^2R^3 , R^2 and R^3 can be combined to form a 5- to 7-membered heterocyclyl ring;

 R^4 is selected from the group consisting of H, (C_1-C_6) alkyl, (C_3-C_6) cycloalkyl, (C_4-C_7) cycloalkyl-alkyl, (C_2-C_6) alkenyl and (C_2-C_6) alkynyl;

A is a substituted or unsubstituted fused carbocyclic or heterocyclic ring system, said ring system being mono- or bicyclic wherein said mono- or bicyclic rings are selected from the group consisting of five- and six-membered rings that are aromatic or partially or completely saturated; and

B is a substituted or unsubstituted five- or six-membered ring which is aromatic or partially or completely saturated, containing at least one nitrogen atom, and from 0 to 3 additional heteroatoms, wherein the B ring substituents are selected from the group consisting of halogen, CF₃, CF₃O, (C₁-C₆)alkyl, perfluoro(C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-C₆)heteroalkyl, (C₁-C₆)alkoxy, (C₁-C₆)thioalkoxy, amino, (C₁-C₆)alkylamino, di(C₁-C₆)alkylamino, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl, cyano, nitro, sulfonamido, (C₁-C₆)acyl, (C₁-C₆)acylamino, (C₁-C₆)alkoxycarbonyl, (C₁-C₆)alkoxycarbonyl(C₁-C₆)alkyl, carboxamido and (C₁-C₆)heteroalkoxy.

92. A method for modulating IKK, comprising contacting a cell with a compound having the formula:

$$\begin{array}{c|c}
R^1 & X \\
R^4 & N \\
\end{array}$$

34 wherein

W and X are independently selected from the group consisting of N and CH;

	0	Y is selected from the group consisting of 0, 5 and N(R);					
	7	wherein R is selected from the group consisting of H, CN, NO ₂ , (C ₁ -					
	8	8 C_{10})alkyl, (C_3-C_{10}) cycloalkyl, (C_4-C_{10}) cycloalkyl-alkyl, (C_3-C_{10})					
	9	C ₁₀)alkenyl and (C ₂ -C ₁₀)alkynyl;					
	10	Z is selected from the group consisting of H, (C ₁ -C ₁₀)alkyl, (C ₃ -C ₁₀)cycloalkyl,					
	11	(C_4-C_{10}) cycloalkyl-alkyl, (C_2-C_{10}) alkenyl, (C_2-C_{10}) alkynyl and NR^2R^3 ;					
	12	R ¹ , R ² and R ³ are independently selected from the group consisting of H, (C ₁ -					
	13	C_{10}) alkyl, (C_3-C_{10}) alkenyl, (C_2-C_{10}) alkynyl, (C_1-C_{10}) heteroalkyl, (C_3-C_{10})					
	14	C_{10})cycloalkyl, (C_4 - C_{10})cycloalkyl-alkyl, (C_3 - C_{10})cycloheteroalkyl-alkyl,					
	15	(C_3-C_{10}) cycloheteroalkyl, aryl, aryl (C_1-C_4) alkyl, aryl (C_1-C_4) heteroalkyl,					
	16	heteroaryl(C_1 - C_4)alkyl, heteroaryl(C_1 - C_4)heteroalkyl and perfluoro(C_1 -					
	17	C ₆)alkyl; and wherein when Z is NR ² R ³ , R ² and R ³ can be combined to					
e E	18	form a 5- to 7-membered heterocyclyl ring;					
4	19	R ⁴ is selected from the group consisting of H, (C ₁ -C ₆)alkyl, (C ₃ -C ₆)cycloalkyl,					
, :	20	(C ₄ -C ₇)cycloalkyl-alkyl, (C ₂ -C ₆)alkenyl and (C ₂ -C ₆)alkynyl;					
	21	A is a substituted or unsubstituted fused carbocyclic or heterocyclic ring system,					
	22	said ring system being mono- or bicyclic wherein said mono- or bicyclic					
	23	rings are selected from the group consisting of five- and six-membered					
	24	rings that are aromatic or partially or completely saturated; and					
	25	B is a substituted or unsubstituted five- or six-membered ring which is aromatic or					
	26	partially or completely saturated, containing at least one nitrogen atom,					
	27	and from 0 to 3 additional heteroatoms, wherein the B ring substituents are					
	28	selected from the group consisting of halogen, CF ₃ , CF ₃ O, (C ₁ -C ₆)alkyl,					
	29	perfluoro(C ₁ -C ₆)alkyl, (C ₂ -C ₆)alkenyl, (C ₂ -C ₆)alkynyl, (C ₁ -C ₆)heteroalkyl,					
	30	(C_1-C_6) alkoxy, (C_1-C_6) thioalkoxy, amino, (C_1-C_6) alkylamino, di (C_1-C_6)					
	31	C ₆)alkylamino, (C ₃ -C ₁₀)cycloalkyl, (C ₄ -C ₁₀)cycloalkyl-alkyl, (C ₃ -					
	32	C ₁₀)cycloheteroalkyl, cyano, nitro, sulfonamido, (C ₁ -C ₆)acyl, (C ₁ -					
	33	C ₆)acylamino, (C ₁ -C ₆)alkoxycarbonyl, (C ₁ -C ₆)alkoxycarbonyl(C ₁ -					
	34	C_6)alkyl, carboxamido and (C_1 - C_6)heteroalkoxy.					
	1	93. The method of Claim 92, wherein said compound is an IKK					
	2	inhibitor.					
	_						

- 94. The method of Claim 92, wherein said compound is an IKK
- 4 activator.
- 1 95. A method for the preparation of antiinflammation agents
- 2 comprising contacting a precursor compound having the formula:

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wherein

W and X are independently selected from the group consisting of N and CH; R⁴ is selected from the group consisting of H, (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, 7 8 9 10 (C₄-C₇)cycloalkyl-alkyl, (C₂-C₆)alkenyl and (C₂-C₆)alkynyl;

A is a substituted or unsubstituted fused carbocyclic or heterocyclic ring system, said ring system being mono- or bicyclic wherein said mono- or bicyclic rings are selected from the group consisting of five- and six-membered rings that are aromatic or partially or completely saturated; and

B is a substituted or unsubstituted five- or six-membered ring which is aromatic or partially or completely saturated, containing at least one nitrogen atom, and from 0 to 3 additional heteroatoms, wherein the B ring substituents are selected from the group consisting of halogen, CF₃, CF₃O, (C₁-C₆)alkyl, perfluoro(C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, (C₁-C₆)heteroalkyl, (C_1-C_6) alkoxy, (C_1-C_6) thioalkoxy, amino, (C_1-C_6) alkylamino, di (C_1-C_6) alkylamino, di (C_1-C_6) alkylamino, di (C_1-C_6) alkylamino, di C₆)alkylamino, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl, cyano, nitro, sulfonamido, (C₁-C₆)acyl, (C₁- C_6)acylamino, (C_2-C_6) alkoxycarbonyl, (C_2-C_6) alkoxycarbonyl (C_1-C_6) alkoxycarbonyl C₆)alkyl, carboxamido and (C₁-C₆)heteroalkoxy

22 with a compound having the formula:

$$R^1$$
 N
 Z
 NH_2

23

wherein 24

25 Y is selected from the group consisting of O, S and N(R);

wherein R is selected from the group consisting of H, CN, NO₂, (C₁-26 27 C₁₀)alkyl, (C₃-C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-28 C₁₀)alkenyl and (C₂-C₁₀)alkynyl; Z is selected from the group consisting of H, (C_1-C_{10}) alkyl, (C_3-C_{10}) cycloalkyl, 29 (C_4-C_{10}) cycloalkyl-alkyl, (C_2-C_{10}) alkenyl, (C_2-C_{10}) alkynyl and NR^2R^3 ; 30 R^{1} , R^{2} and R^{3} are independently selected from the group consisting of H, (C₁-31 C_{10})alkyl, (C_3-C_{10}) alkenyl, (C_2-C_{10}) alkynyl, (C_2-C_{10}) heteroalkyl, (C_3-C_{10}) 32 C₁₀)cycloalkyl, (C₄-C₁₀)cycloalkyl-alkyl, (C₃-C₁₀)cycloheteroalkyl-alkyl, 33 34 (C_3-C_{10}) cycloheteroalkyl, aryl, aryl (C_1-C_4) alkyl, aryl (C_2-C_4) heteroalkyl, 35 heteroaryl(C₂-C₄)alkyl, heteroaryl(C₂-C₄)heteroalkyl and perfluoro(C₁-C₆)alkyl; and wherein when Z is NR²R³, R² and R³ can be combined to 36 37 form a 5- to 7-membered ring; and wherein when Y is N(R), R and R¹ are optionally combined to form a 5- to 7-membered ring; under conditions sufficient to produce compounds having the formula:

wherein each of A, B, R¹, R⁴, W, X, Y and Z have the meanings provided above.

96. A compound having the formula:

3 wherein

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W and X are independently selected from the group consisting of N and CH; R⁴ is selected from the group consisting of H, (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, (C₄-C₇)cycloalkyl-alkyl, (C₂-C₆)alkenyl and (C₂-C₆)alkynyl; A is a substituted or unsubstituted fused carbocyclic or heterocyclic ring system. said ring system being mono- or bicyclic wherein said mono- or bicyclic

9	ri	ings a	re selected from the group consisting of five- and six-membered			
10	ri	rings that are aromatic or partially or completely saturated; and				
11	B is a substituted or unsubstituted five- or six-membered ring which is aromatic or					
12	p	partially or completely saturated, containing at least one nitrogen atom,				
13	a	and from 0 to 3 additional heteroatoms, wherein the B ring substituents are				
14	S	selected from the group consisting of halogen, CF ₃ , CF ₃ O, (C ₁ -C ₆)alkyl,				
15	p	perfluoro(C ₁ -C ₆)alkyl, (C ₂ -C ₆)alkenyl, (C ₂ -C ₆)alkynyl, (C ₁ -C ₆)heteroalkyl, (C ₁ -C ₆)alkoxy, (C ₁ -C ₆)thioalkoxy, amino, (C ₁ -C ₆)alkylamino, di(C ₁ -C ₆)alkylamino, (C ₃ -C ₁₀)cycloalkyl, (C ₄ -C ₁₀)cycloalkyl-alkyl, (C ₃ -				
16	(
17	C					
18	C	C ₁₀)cy	cloheteroalkyl, cyano, nitro, sulfonamido, (C ₁ -C ₆)acyl, (C ₁ -			
19	C	C ₆)acy	lamino, (C ₂ -C ₆)alkoxycarbonyl, (C ₂ -C ₆)alkoxycarbonyl(C ₁ -			
<u></u> 20	C	C ₆)alk	yl, carboxamido and (C_1-C_6) heteroalkoxy.			
1	9	7.	A compound of claim 96, wherein R ⁴ is hydrogen.			
1 1 2 2	$Z ext{ is } NR^2R^3.$	98 .	A compound of claim 96, wherein R ⁴ is hydrogen, Y is O or S, and			
1 2 3		9.	A compound of claim 96, wherein R ⁴ is hydrogen, Y is O or S, Z is			
12	•		as a nitrogen atom at a position two atoms away from the atom			
₹ 3 £	attaching B to th	ne rem	nainder of the molecule.			
1	1	00.	A compound of claim 96, B contains a nitrogen atom at the point of			
2	attachment of B	to the	e remainder of the molecule.			
1	1	01.	A compound of claim 99, wherein B is selected from the group			
2	consisting of 1-	methy	limidazol-5-yl, 1-(trifluoromethyl)imidazol-5-yl, 5-methylimidazol-			
3	1-yl, 5-(trifluoro	meth	yl)imidazol-1-yl, thiazol-5-yl, imidazol-1-yl, 1-methyl-1,3,4-			

triazolyl, and 4-methyl-1,2,4-triazol-3-yl.